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EXAMINER	
JUNG, UNSU	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,320	MANSSON ET AL.	
	Examiner	Art Unit	
	Unsu Jung	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *8-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendments in the reply filed on December 10, 2007 have been fully acknowledged and entered. The reply included amendments to claim 1 and addition of new claims 13 and 14.

2. Claims 1-14 are pending, claims 8-12 have been withdrawn from consideration, and claims 1-7, 13, and 14 are under consideration for their merits.

Rejections Withdrawn

3. Rejection of claims 1-7 under 35 U.S.C. 112, second paragraph and the rejection of claims 1-7 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement have been withdrawn in view of amended independent claim 1 in the reply filed on December 10, 2007:

Claim Rejections - 35 USC § 112, First Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for the invention as now claimed: "the component b) of the monolayer is fully formed when firmly attached to the monolayer."

Applicant's amendment, filed on December 10, 2007 asserts that no new matter has been added. However, Applicant's amendment does not provide sufficient direction for the written description for the above-mentioned "the component b) of the monolayer is fully formed when firmly attached to the monolayer."

Although the specification as originally filed provides support for the monolayer being firmly attached to a metal surface (p3, lines 19-25), the specification as originally filed does not provide support for now claimed "the monolayer being firmly attached to the monolayer."

The specification as filed does not provide a written description or set forth the metes and bounds of this phrase. The specification does not provide blazemarks nor direction for the instant methods encompassing the above-mentioned " the component b) of the monolayer is fully formed when firmly attached to the monolayer" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear

in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the "the component b) of the monolayer is fully formed when firmly attached to the monolayer" indicated above.

See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112, Second Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the phrase "the component b) of the monolayer is fully formed when firmly attached to the monolayer." It is unclear how the monolayer can be firmly attached to itself. According to claim 1, from which claim 14 depends, the monolayer is firmly attached to the metal surface and not to the monolayer itself. Therefore, there is inconsistent antecedent basis as claim 1 recites that the monolayer is firmly attached to the metal surface and not to the monolayer itself as recited in claim 14. For the purpose

of examination, the phrase has been interpreted in light of the specification (p3, lines 19-25), which discloses that the monolayer is firmly attached to the metal surface.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 2, 6, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (WO 00/43774, July 27, 2000) in view of Svedhem et al. (*J. Org. Chem*. 2001, Vol. 66, pp4494-4503) and Bentley et al. (U.S. PG Pub. No. US 2001/0027212 A1, Oct. 4, 2001).

Willner et al. teaches a sensitive method of detecting small amount of low molecular weight compounds (typically below about 1,500 Daltons), which includes explosive molecules such as dinitrotoluene (DNT) and TNT (derivatized explosives, see entire document, particularly Fig's 1A and 1B) and drugs such as heroin and cocaine (narcotics, p5, lines 1-15) using quartz crystal microbalance (QCM). Willner et al. further teaches that any method intended for sensing the presence of explosive molecules or other types of low molecular weight molecules such as drugs should be highly sensitive and adapted for detecting a small amount of molecules. The QCM includes a piezoelectric crystal sandwiched between two gold electrodes (Abstract and p23, lines 14-17) coated with an antigen, which is then contacted with an antibody (p24, lines 8-12). Measurement of resonance frequency at this stage yields a certain basic frequency (p24, lines 9-12). Challenging the electrode with a sample comprising antigens causes release of some of the antibodies to yield a soluble antigen-antibody complex (antigens reversibly bound to antibodies specific for the antigens), which

reduces the immobilized mass and consequently the frequency is increased as a result of and signifies the presence of the assayed molecule in the medium (p24, lines 13-19).

With respect to claim 2, Willner et al. teaches a coated gold surface (gold electrode) on a solid support (Abstract and p23, lines 14-17).

With respect to claim 6, Willner et al. teaches a coated metal surface on a solid support, wherein the solid support is piezoelectric crystal sandwiched between two gold electrodes (Abstract and p23, lines 14-17).

With respect to claim 13, Willner et al. teaches that the antigens are reversibly bound to antibodies specific for analyte antigens, which antibodies are easily detachable in a displacement reaction (p24, lines 7-19).

However, Willner et al. fails to teach a coated metal surface further comprising a self-assembled monolayer (SAM) of oligo(ethylene glycol)-terminated (OEG-terminated) alkanethiol amides.

Svedhem et al. teaches a self-assembled monolayer (SAM) of oligo(ethylene glycol)-terminated (OEG-terminated) alkanethiol amides on gold coated surface on a solid support (see entire document, particularly p4503, right column, *Preparation of SAMs*) designed to address structure and stability of biosensing interfaces (Abstract). SAM-forming OEG molecules includes alkyl portion of the alkanethiols having 2, 5, 11, and 15 CH_2 groups (methylene groups) and OEG portion has 1, 2, 4, 6, 8, 10, and 12 (CH_2CH_2O) (ethylene oxy) units (Abstract). Organic modifications of gold surfaces by SAMs have proven to be successful in biosensor applications (p4494, *Introduction*, second paragraph). Furthermore, ethylene glycols provide good anchors for biological

receptors and ligands and reduce nonspecific binding of proteins and other bioactive molecules (p4494, *Introduction*, first paragraph). Poly(ethylene glycol) derivatives are also ideal as spacer candidates because they are inexpensive, water soluble, stable, and available in a wide range of molecular weight distributions (p4494, *Introduction*, first paragraph). Svedhem et al. further teaches that the PEG derivatives (OEG-terminated alkanethiol amides) can be used as spacer molecules (p4494, *Introduction*, first paragraph) as closely packed ligands attached to the OEG-terminated alkanethiol amides would become less accessible to binding due to sterical hindrance (p4494, *Introduction*, second paragraph).

With respect to claim 7, Svedhem et al. teaches OEG having 4-6 ethylene oxy units and the alkyl group having 15 methylene units (Abstract).

With respect to claim 14, Svedhem et al. teaches a monolayer (spacer layer) that is protein repellent (reducing nonspecific protein binding) and the component b) of the monolayer that is fully formed when attached to the metal surface (Abstract and p4494, *Introduction*, first paragraph).

However, Svedhem et al. fails to teach low molecular weight antigens bound via an amide group to the SAM-forming OEG molecules.

Bentley et al. teaches that conventional amide linkages formed between amine groups on drugs, which include peptides, proteins and small agents (antigens), having amine groups and PEG through non-hydrolyzable amide linkages, which are generally stable (see entire document, particularly p1, paragraph [0007]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ mixed SAM of OEG-terminated alkanethiol amides with and without attached ligands as taught by Svedhem et al. in the QCM biosensor of Willner et al. in order to provide a biosensing interface with structurally stable SAM, which reduce nonspecific binding of proteins and other bioactive molecules. The advantage of having a structurally stable SAM, which has the characteristic of reducing nonspecific binding of proteins and other bioactive molecules and reduces sterical hindrance provides the motivation to include the SAM of OEG-terminated alkanethiol amides of Svedhem et al. in the QCM biosensor of Willner et al. with a reasonable expectation of success since the solid support of Willner et al. includes a gold coated surface and Svedhem et al. teaches that he SAM of OEG-terminated alkanethiol amides can be formed on gold coated surfaces for use as a biosensing interfaces. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to use conventional amide linkages formed between amine groups on drugs and ethylene glycol of OEG as taught by Bentley et al. in order to immobilize antigens of interest on the SAM of OEG-terminated alkanethiol amides of Svedhem et al. as the amide linkages are generally stable and non-hydrolyzable. The advantage of amide linkages, which are stable and non-hydrolyzable provides the motivation to employ amide linkages to immobilize antigens of Willner et al. on the SAM of OEG-terminated alkanethiol amides of Svedhem et al. with a reasonable expectation of success as Bentley et al. teaches that small molecules such as drugs can be immobilized to ethylene glycols of PEG, which are also present in OEGs.

12. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (WO 00/43774, July 27, 2000) in view of Svedhem et al. (*J. Org. Chem.* 2001, Vol. 66, pp4494-4503) and Bentley et al. (U.S. PG Pub. No. US 2001/0027212 A1, Oct. 4, 2001) as applied to claim 1 above, and further in view of Duffy (U.S. PG Pub. No. US 2002/0028463 A1, Mar. 7, 2002).

Willner et al. in view of Svedhem et al. and Bentley et al. teaches a coated metal surface on a solid support as set forth in item 11 above. Willner et al. further teaches that antigens are selected from a group consisting of explosives and narcotics (p5, lines 1-15).

With respect to claim 4, Willner et al. teaches derivatized explosives, which include TNT and DNT (Fig's 1A and 1B). The derivatized DNT includes an amine group, which can form an amide linkage with ethylene glycol of OEG.

With respect to claim 5, Willner et al. teaches antigens are selected from cocaine and heroine (p5, lines 13-15).

However, Willner et al. in view of Svedhem et al. and Bentley et al. fails to teach a coated metal surface on a solid support, wherein the antigens are bound to the same or different monolayers in patches on the solid support.

Duffy teaches an array system which can be used to elucidate interactions between molecules (see entire document, particularly p5, paragraph [0039]). The system comprises array of binding areas (patches) for immobilizing biomolecules and provides for high throughput, as many interactions may be tested in a single assay (p5,

paragraphs [0040] and [0041]). Duffy further teaches that the interactions between molecules can be detected using QCM (p13, paragraph [0113]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include an array of binding patches for immobilization of antigens of the Willner et al. in view of Svedhem et al. and Bentley et al. as taught by Duffy in order to perform high throughput analysis of many interactions, which may be tested in a single assay. The advantage of having the capacity to perform high throughput analysis of many interactions, which may be tested in a single assay, provides the motivation to include an array of binding patches for immobilization of antigens of the Willner et al. in view of Svedhem et al. and Bentley et al.. Further, one of ordinary skill in the art would have had a reasonable expectation of success since Duffy teaches that the array system can be used with QCM detection methods to detect binding interaction on the array surface.

Response to Arguments

13. Rejection of claims 1, 2, 6, and 7 under 35 U.S.C. 103(a) as being unpatentable over Willner et al. in view of Svedhem et al. and Bentley et al.

Applicant's arguments filed on December 10, 2007 have been fully considered, but they are not persuasive essentially for the reasons of record and arguments addressed herein.

Applicant's argument regarding Willner et al.'s lack of teaching any other capturing agent than cystamine (p6 of the Remarks) has been fully considered, but is not found persuasive essentially for the reasons of record. Although, Willner et al. fails

to teach a metal surface coated with a capturing agent comprising self-assembled monolayer (SAM) of oligo(ethylene glycol)-terminated (OEG-terminated) alkanethiol amides, , it would have been obvious to one of ordinary skill in the art at the time of the invention to employ mixed SAM of OEG-terminated alkanethiol amides with and without attached ligands as taught by Svedhem et al. in the QCM biosensor of Willner et al. in order to provide a biosensing interface with structurally stable SAM, which reduce nonspecific binding of proteins and other bioactive molecules. The advantage of having a structurally stable SAM, which has the characteristic of reducing nonspecific binding of proteins and other bioactive molecules and reduces sterical hindrance provides the motivation to include the SAM of OEG-terminated alkanethiol amides of Svedhem et al. in the QCM biosensor of Willner et al. with a reasonable expectation of success since the solid support of Willner et al. includes a gold coated surface and Svedhem et al. teaches that he SAM of OEG-terminated alkanethiol amides can be formed on gold coated surfaces for use as a biosensing interfaces.

Applicant's argument regarding OEG terminated with carboxylic acid (pp6-9) has been fully considered but is not found persuasive essentially for the reasons of record. As stated in item 14 of Office Action dated August 8, 2007, Svedhem et al. teaches that the SAM comprises OEG-terminated alkanethiol amides on gold coated surfaces (see entire document, particularly p4503, right column, *Preparation of SAMs*). SAM-forming OEG molecules includes alkyl portion of the alkanethiols having 2, 5, 11, and 15 CH_2 groups (methylene groups) and OEG portion has 1, 2, 4, 6, 8, 10, and 12 (CH_2CH_2O) (ethylene oxy) units (Abstract). Further, Svedhem et al. teaches the PEG derivatives

(OEG-terminated alkanethiol amides) can be used as spacer molecules (p4494, *Introduction*, first paragraph) as closely packed ligands attached to the OEG-terminated alkanethiol amides would become less accessible to binding due to sterical hindrance (p4494, *Introduction*, second paragraph). Therefore, one of ordinary skill in the art would recognize that OEG-terminated alkanethiol amides, which do not contain biological receptors/ligands would be mixed with OEG-terminated alkanethiol amides attached to biological receptors/ligands to form SAM on gold coated surfaces in order to provide space between biological receptors/ligands, which would reduce sterical hindrance and facilitate binding of receptors and ligands.

Applicant's argument regarding antigens reversibly bound to antibodies specific for analyte antigens and the antibodies being easily detachable in a displacement reaction has been fully considered but is not found persuasive as Willner et al. teaches that the antigens are reversibly bound to antibodies specific for analyte antigens, which antibodies are easily detachable in a displacement reaction (p24, lines 7-19) as set forth in item 11 above.

Taken together, Willner et al. in view of Svedhem et al. and Bentley et al. teaches all the limitations of the claimed invention having mixture of SAM (OEG-terminated amide group-containing alkyl thiols) with or without bioactive molecules (drugs/explosives) on a solid metal support.

14. Rejection of claims 3-5 under 35 U.S.C. 103(a) as being unpatentable over Willner et al. in view of Svedhem et al. and Bentley et al., and further in view of Duffy

Applicant's arguments filed on October 30, 2006 have been fully considered but they are not persuasive in view of previously stated grounds of rejection and reasons set forth in item 13 above.

15. Since the prior art fulfills all the limitations currently recited in the claims, the invention as currently recited would read upon the prior art.

Conclusion

16. No claim is allowed.

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is (571)272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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